Hypertonic saline

Hypertonic saline is a crystalloid intravenous fluid composed of NaCl dissolved in water with a higher concentration of sodium compared to normal blood serum. Both 3% and 5% hypertonic saline (HS) is currently FDA-approved for use in hyponatremia and increased intracranial pressure (ICP). Patients with hyponatremia with severe features should have their serum sodium gradually corrected with boluses of hypertonic saline. Patients should have their serum sodium monitored at regular intervals and can receive multiple boluses a day.

Hypertonic saline should be discontinued once the patient's symptoms improve or they have an adequate increase in serum sodium. Cerebral edema and elevated intracranial pressure (ICP) are significant causes of morbidity and mortality in patients with intracranial tumors, cerebral hematomas, traumatic brain injuries, cerebral infarcts, and intracranial hemorrhages. Hypertonic saline increases the osmolarity of the blood, which allows fluid from the extravascular space to enter the intravascular space, which leads to decreases in brain edema, improved cerebral blood flow, and decreased CSF production. Research shows that 3% hypertonic saline decreases ICP similarly to 20% mannitol.

Both hypertonic fluids have similar effects on hemodynamics. Hypertonic saline leads to increases in serum sodium and has less of a diuretic effect than mannitol likely due to the increased serum sodium causing ADH release. Hypertonic saline administered after mannitol in traumatic brain injury has also been shown to improve cerebral oxygenation in addition to lowering ICP.

Due to there being no guidelines regarding the administration of hypertonic saline for increased ICP, various studies have used concentrations of 3% to 23.5% NaCl.

While not FDA-approved, small doses of hypertonic saline are thought to be effective in hypovolemia and shock due to the movement of fluid from the intracellular to intravascular spaces, increasing intravascular fluid volume and improving capillary blood flow [1].

Hypertonic saline emerged as an alternative to mannitol [2] , and gained increasing clinical interest due to its reported efficacy in treating cerebral edema and elevated intracranial pressure [3] [4].

Early data suggest that indications for each agent may ultimately depend on ICP etiology [5].

Hypertonic saline avoids the diuretic effect of mannitol while still being effective at reducing brain water. After administration, cerebral perfusion may actually be increased [6].

Mannitol and hypertonic saline are routinely employed as hyperosmolar therapy in North America. Specific circumstances may prompt selection of a specific agent. Hypertonic saline administration may be hazardous in hyponatremia [7].

Serum sodium values did not significantly change more than 10h after infusion of HS. Further studies are needed to determine the optimal frequency of routine sodium checks to increase the quality of care and decrease healthcare costs [8].

Bolus dosing of hypertonic saline was first studied and documented 1919 by Weed and McKibben [9].

Various concentrations are clinically used, with as much as 30 mL boluses of 23.4% saline in a single dose. Rapid increases in serum sodium in this setting do not appear to cause the neurological complications that may be encountered in the context of rapid correction of hyponatremia [10].

Hypertonic saline has attributes beyond those expected for a simple osmotherapeutic agent. It affects the vasoregulatory, immunomodulatory, and neurochemical environment of the brain and the blood–brain barrier in ways that may benefit different categories of brain injury [11] [12] [13].

Hypertonic saline (HTS) provides better brain relaxation than mannitol during elective intracranial tumor surgery [14].

Case series

2003

Twenty consecutive patients with head trauma and persistent coma who required infusions of an osmotic agent to treat episodes of intracranial hypertension resistant to well-conducted standard modes of therapy were studied. Intracranial hypertension was considered refractory when it persisted despite deep sedation, optimal hemodynamic status, and, in some patients, drainage of cerebral spinal fluid.

INTERVENTIONS: Patients were randomly assigned to receive isovolume infusions of either 7.5% hypertonic saline solution (2400 mOsm/kg/H(2)O) or 20% mannitol (1160 mOsm/kg/H(2)O). The patients were given 2 mL/kg (body weight) of either solution, i.e., 361 +/- 13 mOsm of saline or 175 +/- 12 mOsm of mannitol per injection.

MEASUREMENTS AND MAIN RESULTS: The main variables studied were the number and the duration of episodes of intracranial hypertension per day during the study period, which was stopped after the last episode of intracranial hypertension was recorded from intracranial pressure monitoring or after the allocated treatment failure. Patients in the HHS group were monitored for 7 +/- 5 days and those in the mannitol group for 7 +/- 6 days (not significant). The rate of failure for each treatment was also evaluated. Failure was defined as the persistence of intracranial hypertension despite two successive infusions of the same osmotic agent. The mean number of osmotic solute infusions was 3.7 +/- 5.3 in the mannitol group and 3.3 +/- 4.1 in the hypertonic saline solution group (not significant). The mean number (6.9 +/- 5.6 vs. 13.3 +/- 14.6 episodes) of intracranial hypertension episodes per day and the daily duration (67 +/- 85 vs. 131 +/- 123 min) of intracranial hypertension episodes were significantly lower in the hypertonic saline solution group ($p < .01$). The rate of clinical failure was also significantly lower in the hypertonic saline solution group: 1 of 10 patients vs. 7 of 10 patients ($p < .01$).

In this study, when a hypertonic solute was required for the treatment of refractory intracranial hypertension episodes in patients with severe head trauma, increasing the osmotic load by giving 2 mL/kg (body weight) of 7.5% saline (361 +/- 13 mOsm) was more effective than giving 2 mL/kg (body weight) of 20% mannitol (175 +/- 12 mOsm). Within the limitations of the present study, these data suggest that giving 2 mL/kg hypertonic saline solution (approximately 480 mOsm/70 kg body weight) is an effective and safe initial treatment for intracranial hypertension episodes in head-trauma patients when osmotherapy is indicated [15].

1999

Qureshi et al. performed a retrospective chart review of all patients admitted with severe head injury, defined as admission Glasgow Coma Scale score of 8 or less, in the neurocritical care unit of a University hospital. Intravenous infusion of 2% or 3% saline/acetate for treatment of cerebral edema was introduced in the unit in April of 1993. The clinical characteristics, interventions required, and outcomes in patients who received HS were compared with patients who received 0.9% saline infusion only. Multivariate analyses were used to evaluate the impact of HS use on in-hospital mortality and Glasgow Outcome Scale score at discharge.

Thirty-six patients with cerebral edema caused by head trauma received infusion of HS initiated within 48 hours of admission for a mean period of 72 +/- 85 hours. Compared with 46 patients who did not receive HS, there were no differences observed in age and admission Glasgow Coma Scale scores. Patients who received HS were more likely to have a penetrating injury ($p = 0.07$) and a mass lesion on initial computed tomographic scan ($p = 0.07$). There was no difference between frequency of use of hyperventilation, mannitol, cerebrospinal fluid drainage, and vasopressors between the two groups. The requirement for pentobarbital coma was higher in HS group ($n = 7$ patients) versus control group ($n = 2$,$p = 0.04$). After adjusting for differences between both groups, infusion of HS was associated with higher in-hospital mortality (OR, 3.1; 95% CI, 1.1-10.2).

HS administration as prolonged infusion does not seem to favorably impact on requirement for other interventions and in-hospital mortality in our experience. Further efforts should be directed toward use of HS as bolus administrations or short infusions [16].

1998

Thirty-four patients were enrolled and were similar in age and Injury Severity Score. HTS patients had a lower admission Glasgow Coma Scale score (HTS: 4.7+/-0.7; LRS: 6.7+/-0.7; $p = 0.057$), a higher initial ICP (HTS: 16+/-2; LRS: 11+/-2; $p = 0.06$), and a higher initial mean maximum ICP (HTS: 31+/-3; LRS: 18+/-2; $p < 0.01$). Treatment effectively lowered ICP in both groups, and there was no significant difference between the groups in ICP at any time after entry. HTS patients required significantly more interventions (HTS: 31+/-4; LRS: 11+/-3; $p < 0.01$). During the study, the change in maximum ICP was positive in the LRS group but negative in the HTS group (LRS: +2+/-3; HTS: -9+/-4; $p < 0.05$).

As a group, HTS patients had more severe head injuries. HTS and LRS used with other therapies effectively controlled the ICP. The widely held conviction that sodium administration will lead to a sustained increase in ICP is not supported by this work [17].

Metaanalysis

A wealth of evidence from randomized controlled trials (RCTs) has indicated that hypertonic saline (HS) is at least as effective as, if not better than, mannitol in the treatment of increased intracranial pressure (ICP). However, there is little known about the effects of HS in patients during neurosurgery. Thus, a meta-analysis was performed to compare the intraoperative effects of HS with mannitol in patients undergoing craniotomy.

PUBMED, EMBASE and Cochrane Central Register of Controlled Trials, internet-based clinical trial registries and conference proceedings were searched.

The outcomes included intraoperative brain relaxation, intraoperative ICP, total volume of fluid required, diuresis, hemodynamic parameters, electrolyte level, mortality or dependence and adverse events.

Seven RCTs with 468 participants were included. The quality of the included trials was acceptable. HS could significantly increase the odds of satisfactory intraoperative brain relaxation (OR: 2.25, 95% CI: 1.32-3.81; P = 0.003) and decrease the mean difference (MD) of maximal ICP (MD: -2.51mmHg, 95% CI: -3.39-1.93mmHg; P<0.00001) in comparison with mannitol with no significant heterogeneity among the study results. Compared with HS, mannitol had a more prominent diuretic effect. And patients treated with HS had significantly higher serum sodium than mannitol-treated patients.

Considering that robust outcome measures are absent because brain relaxation and ICP can be influenced by several factors except for the hyperosmotic agents, the results of present meta-analysis should be interpreted with cautions. Well-designed RCTs in the future are needed to further test the present results, identify the impact of HS on the clinically relevant outcomes and explore the potential mechanisms of HS [18)].

Hypertonic saline for aneurysmal subarachnoid hemorrhage

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